

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:  
 CHRISTOPHER B. LINDER  
 THOMAS, KAYDEN, HORSTEMEYER & RISLEY, LLP  
 100 GALLERIA PARKWAY, N.W.  
 SUITE 1750  
 ATLANTA, GA 30339-5948

## PCT

### NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing (day/month/year)	<b>08 NOV 2004</b>
Applicant's or agent's file reference 050508-2370	<b>FOR FURTHER ACTION</b> See paragraphs 1 and 4 below
International application No. PCT/US04/37090	International filing date (day/month/year) 08 November 2004 (08.11.2004)

Applicant  
EMORY UNIVERSITY

<p>1. <input checked="" type="checkbox"/> The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.</p> <p><b>Filing of amendments and statement under Article 19:</b>          The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):</p> <p><b>When?</b> The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.</p> <p><b>Where?</b> Directly to the International Bureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Facsimile No.: +41 22 740 14 35</p> <p><b>For more detailed instructions</b>, see the notes on the accompanying sheet.</p>	<p>2. <input type="checkbox"/> The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.</p> <p>3. <input type="checkbox"/> <b>With regard to the protest against payment of (an) additional fee(s) under Rule 40.2</b>, the applicant is notified that:</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.</li> <li><input type="checkbox"/> no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.</li> </ul> <p>4. <b>Reminders</b>          Shortly after the expiration of <b>18 months</b> from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.</p> <p>The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.</p> <p>Within <b>19 months</b> from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase <b>until 30 months</b> from the priority date (in some Offices even later); otherwise, the applicant must, <b>within 20 months</b> from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.</p> <p>In respect of other designated Offices, the time limit of <b>30 months</b> (or later) will apply even if no demand is filed within 19 months.</p> <p>See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the <i>PCT Applicant's Guide</i>, Volume II, National Chapters and the WIPO Internet site.</p>
<p>Name and mailing address of the ISA/ US          Mail Stop PCT, Attn: ISA/US          Commissioner for Patents          P.O. Box 1450          Alexandria, Virginia 22313-1450          Facsimile No. (703) 305-3230</p>	<p>Authorized officer  <i>Rebecca J. Foley</i>          Telephone No. 703-308-1235</p> <p style="text-align: right;"><i>Christopher B. Linder</i></p>

Form PCT/ISA/220 (January 2004) (See notes on accompanying sheet)

Comment on Abstract due DUE 12/8/05

ISPR RESPONSE DUE 11/8/06

Demand due from transmittal date due 12/8/06

THOMAS, KAYDEN  
 HORSTEMEYER & RISLEY, LLP.

NOV 14 2005

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:  
**CHRISTOPHER B. LINDER**  
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 SUITE 1750  
 ATLANTA, GA 30339-5948

**PCT**

**NOTIFICATION OF TRANSMITTAL OF  
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 THE WRITTEN OPINION OF THE INTERNATIONAL  
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(PCT Rule 44.1)

<p>Applicant's or agent's file reference 050508-2370</p> <p>International application No. PCT/US04/37090</p> <p>Applicant EMORY UNIVERSITY</p>	<p>Date of mailing (day/month/year)</p> <p><b>FOR FURTHER ACTION</b> See paragraphs 1 and 4 below</p> <p>International filing date (day/month/year) 08 November 2004 (08.11.2004)</p>
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1.  The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

**When?** The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

**Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes  
1211 Geneva 20, Switzerland, Facsimile No.: +41 22 740 14 35

**For more detailed instructions**, see the notes on the accompanying sheet.

2.  The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3.  **With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:**

the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

<p>Name and mailing address of the ISA/ US          Mail Stop PCT, Attn: ISA/US          Commissioner for Patents          P.O. Box 1450          Alexandria, Virginia 22313-1450          Facsimile No. (703) 305-3230</p>	<p>Authorized officer            Rebecca L. Linder          Telephone No. 703-308-1235</p>
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Form PCT/ISA/220 (January 2004)

(See notes on accompanying sheet)

THOMAS, KAYDEN  
 HORSTEMEYER & RISLEY, LLP.

NOV 14 2005

**SCANNED**

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 050508-2370	<b>FOR FURTHER ACTION</b> <small>see Form PCT/ISA/220 as well as, where applicable, item 5 below.</small>	
International application No. PCT/US04/37090	International filing date (day/month/year) 08 November 2004 (08.11.2004)	(Earliest) Priority Date (day/month/year) 07 November 2003 (07.11.2003)
Applicant EMORY UNIVERSITY		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the Report**
  - a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
    - The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
  - b.  With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.
2.  **Certain claims were found unsearchable** (See Box No. II)
3.  **Unity of invention is lacking** (See Box No. III)
4. With regard to the **title**,
  - the text is approved as submitted by the applicant.
  - the text has been established by this Authority to read as follows:
5. With regard to the **abstract**,
  - the text is approved as submitted by the applicant.
  - the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. With regard to the **drawings**,
  - a. the figure of the **drawings** to be published with the abstract is Figure No. 1
    - as suggested by the applicant.
    - as selected by this Authority, because the applicant failed to suggest a figure.
    - as selected by this Authority, because this figure better characterizes the invention.
  - b.  none of the figures is to be published with the abstract.

## INTERNATIONAL SEARCH REPORT

1

PCT/US04/37090

### Box IV TEXT OF THE ABSTRACT (Continuation of Item 5 of the first sheet)

Methods of treating cancers or tumor, chemopreventative methods of prophylactically treating cancers or tumors, pharmaceutical compositions, methods for the treatment or prevention of a hypoxia-related pathology, methods of modulating HIF-1 activity in a cell, methods of downregulating HIF-1 activity in a cell, methods of treating or preventing cancer or a tumor in a host, and methods of modulating gene transcription in a cell are described. Figure 1 illustrates an embodiment of a beta-diketone compound.

# INTERNATIONAL SEARCH REPORT

PCT/US04/37090

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 31/315  
US CL : 514/494

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 514/494

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
REGISTRY, HCAPLUS, MEDLINE, CANCERLIT, BIOSIS, EMBASE, JAPIO, JICST-EPLUS, USPATFULL

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Database HCAPLUS on STN (Columbus, OH, USA) DN 137:273183, HARRIS<W et al, 'Use of dibenzoylmethane type compounds for treating cancer and cancer-related conditions,' WO 2002078444, 10 Oct 2002, abstract.	1-33

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

01 October 2005 (01.10.2005)

Date of mailing of the international search report

18 NOV 2005

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Rebecca Chot

Telephone No. 703-308-1235

# PATENT COOPERATION TREATY

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INTERNATIONAL SEARCHING AUTHORITY

To:  
CHRISTOPHER B. LINDER  
THOMAS, KAYDEN, HORSTEMEYER & RISLEY, LLP  
100 GALLERIA PARKWAY, N.W.  
SUITE 1750  
ATLANTA, GA 30339-5948

**PCT**

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference  050508-2370		Date of mailing (day/month/year) <b>18 NOV 2005</b>
International application No.  PCT/US04/37090	International filing date (day/month/year)  08 November 2004 (08.11.2004)	Priority date (day/month/year)  07 November 2003 (07.11.2003)
International Patent Classification (IPC) or both national classification and IPC  IPC(7): A61K 31/315 and US Cl.: 514/494		
Applicant  EMORY UNIVERSITY		

1. This opinion contains indications relating to the following items:

<input checked="" type="checkbox"/>	Box No. I Basis of the opinion
<input type="checkbox"/>	Box No. II Priority
<input type="checkbox"/>	Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
<input type="checkbox"/>	Box No. IV Lack of unity of invention
<input checked="" type="checkbox"/>	Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
<input type="checkbox"/>	Box No. VI Certain documents cited
<input type="checkbox"/>	Box No. VII Certain defects in the international application
<input type="checkbox"/>	Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US  Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450  Facsimile No. (703) 305-3230	Authorized officer  <i>Rebecca Cook</i> Telephone No. 703-308-1235
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WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International appl

PCT/US04/3769C

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

a sequence listing  
 table(s) related to the sequence listing

b. format of material

in written format  
 in computer readable form

c. time of filing/furnishing

contained in international application as filed.  
 filed together with the international application in computer readable form.  
 furnished subsequently to this Authority for the purposes of search.

3.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International appl  
PCT/US04/37090

**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Claims <u>1-33</u>	YES
	Claims <u>NONE</u>	NO
Inventive step (IS)	Claims <u>1-33</u>	YES
	Claims <u>NONE</u>	NO
Industrial applicability (IA)	Claims <u>1-33</u>	YES
	Claims <u>NONE</u>	NO

**2. Citations and explanations:**

Claims 1-33 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the instant method for treating cancer or a tumor, downregulating HIF-1 activity in a cell or modulating gene transcription in a cell comprising administering a bidentate zinc chelate or a composition comprising said chelate.

Claims 1-33 meet the criteria set out in PCT Article 33(4), and thus find industrial applicability because the subject matter claimed can be made or used in industry.

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article," "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the international application may be amended ?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Preliminary Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

**When ?** Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments ?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

**How ?** Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

**The amendments must be made in the language in which the international application is to be published.**

#### What documents must/may accompany the amendments ?

##### Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

**The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.**

From the INTERNATIONAL BUREAU

## PCT

NOTIFICATION CONCERNING  
TRANSMITTAL OF COPY OF INTERNATIONAL  
APPLICATION AS PUBLISHED OR REPUBLISHED

To:

LINDER, Christopher, B.  
 Thomas, Kayden, Horstemeyer & Risley, LLP  
 100 Galleria Parkway, N.W.  
 Suite 1750  
 Atlanta, GA 30339  
 ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 26 May 2005 (26.05.2005)
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Applicant's or agent's file reference 050508-2370
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## IMPORTANT NOTICE

International application No. PCT/US2004/037090	International filing date (day/month/year) 08 November 2004 (08.11.2004)	Priority date (day/month/year) 07 November 2003 (07.11.2003)
Applicant EMORY UNIVERSITY et al		

The International Bureau transmits herewith the following documents:

copy of the international application as published by the International Bureau on 26 May 2005 (26.05.2005) under No. WO 2005/046595

copy of international application as republished by the International Bureau on under No. WO

For an explanation as to the reason for this republication of the international application, reference is made to INID codes (15), (48) or (88) (*as the case may be*) on the front page of the attached document.

DOCKETED

THOMAS, KAYDEN  
HORSTEMEYER & RISLEY, L.L.P.

JUN 03 2005

The International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland

Authorized officer

Athina Nickitas-Etienne

Facsimile No.+41 22 338 89 95

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